

Bibliography*: Collagen-based Dressings for Chronic Wound Management

*Selected, quality filtered, not subject to external review

Issue: Congress requested a response regarding VHA's position on the use of collagen-based products in wound care, specifically their role in decreasing amputations. Patients at greatest risk for amputation include those with diabetes, peripheral vascular disease and end stage renal disease. VHA Office of Patient Care Services, charged with responding to the request, asked the VATAP to perform a literature search for evidence that collagen based wound care products improve healing time for patients with foot ulcers.

Methods: VATAP queried the International Network of Agencies for Health Technology Assessment (INAHTA) and the evidence-based health care communities via electronic mail for relevant completed or ongoing technology assessments. In addition, thorough searches were performed of the Cochrane Library, 2002, issue 4, and the HTA database (www.inahta.org) using search terms for wound, chronic, diabetes, and dressing for publications in English. These queries resulted in two completed systematic reviews on wound care from the UK (Bradley et al. 1999; O'Meara et al. 2000) that were relevant to the topic. These reviews were broader in scope than VATAP's assignment to look at collagen products for chronic wounds of the lower extremity, but both reviews included studies of collagen-based products.

Using the methods in these reviews as the basis for its response, VATAP updated and narrowed their search strategies to identify articles reporting research on collagen-based products through November 2002. VATAP searched MEDLINE, EMBASE, BIOSIS, Science Citation Index, Current Contents, Dissertation Abstracts, EconLit, and FEDRIP (Federal Research in Progress). Search terms for specific collagen products were used: Hycure? , Fibracol? , Catrix? , Graftskin or Apligraf? along with the Medical Subject Headings and free text equivalents for collagen alginates, wound dressings, wound healing, diabetic foot, or foot ulcers crossed with terms for randomized controlled trials, controlled trials, blinding, randomization, clinical trials, comparative study, systematic reviews, or meta-analysis.

VATAP hand searched the reference lists of all retrieved articles. In all, the search identified 563 citations. VATAP applied inclusion criteria similar to those in the UK reviews but excluded citations published in languages other than English and redundant citations that were duplicated or superseded by larger or more complete publications by the same investigator group for the same purpose.

Results: VATAP retrieved 19 citations that were relevant to the topic. Eleven met inclusion criteria and are listed in the accompanying bibliography (one proprietary systematic review, ten primary studies). Ten of the reports addressed one of two types of collagen-based dressings: Apligraf? (graftskin) or Promogran matrix wound dressing. VATAP also uncovered one background article on diabetes care in VHA relevant to the topic.

The bibliography is organized by the systematic reviews from the UK, citations about Apligraf? (graftskin), citations about Promogran matrix wound dressing, and one additional citation on VA diabetes care.

Systematic Reviews From the UK on Chronic Wound Management That Include Collagen-Based Products

Bradley M, Cullum N, Nelson EA, Petticrew M, Sheldon T, Torgerson D. Systematic reviews of wound care management: (2) Dressings and topical agents used in the healing of chronic wounds. *Health Technol Assess* 1999;3(17 Pt 2).

O'Meara S, Cullum N, Majid M, Sheldon T. Systematic reviews of wound care management: (3) antimicrobial agents for chronic wounds; (4) diabetic foot ulceration. *Health Technol Assess* 2000;4(21).

Citations About Apligraf? (Graftskin)

Apligraf? (graftskin) is a bioengineered living skin equivalent that consists of a dermal layer of allogenic human fibroblast cells and type I bovine collagen cells and an epidermal layer of allogenic human keratinocyte cells. It is produced by Organogenesis, Inc. (Canton, MA) and is licensed by Novartis Pharmaceutical Corp. (East Hanover, NJ). Apligraf? is FDA-approved for use with: 1) standard therapeutic compression for the treatment of non-infected partial and full-thickness skin ulcers due to venous insufficiency of greater than one month duration and which have not adequately responded to conventional ulcer therapy; and 2) standard diabetic foot ulcer care for the treatment of full-thickness neuropathic diabetic foot ulcers of greater than three weeks duration which have not adequately responded to conventional ulcer therapy and which extend through the dermis but without tendon, muscle, capsule or bone exposure.

<http://www.fda.gov/cdrh/pma/pmanov01.html>

Graftskin for the treatment of skin ulcers. Tecnologica MAP supplement Blue Cross and Blue Shield Association Medical Advisory Panel, 2001; 10-13. Systematic review. Proprietary. Contact Claudia Bonnell at the Blue Cross Blue Shield Association Technology Evaluation Center for information claudia.bonnell@wro.BCBSA.com.

Falanga V, Margolis D, Alvarez O, Auletta M, Maggiasimo F, Altman M, et al. Rapid healing of venous ulcers and lack of clinical rejection with an allogeneic cultured human skin equivalent. Human Skin Equivalent Investigators Group. Arch Dermatol, 1998; 134: 293-300. Comments in:

- Arch Dermatol. 1998 Mar;134(3):344-9
- Arch Dermatol. 1998 Nov;134(11):1483-4

Falanga V, Sabolinski M. A bilayered living skin construct (APLIGRAF(R)) accelerates complete closure of hard-to-heal venous ulcers. *Wound Repair and Regeneration*, 1999; 7: 201-207.

Veves A, Falanga V, Armstrong DG, Sabolinski ML. Graftskin, a human skin equivalent, is effective in the management of noninfected neuropathic diabetic foot ulcers: A prospective randomized multicenter clinical trial. *Diabetes Care*, 2001; 24: 290-295.

Schonfeld WH, Villa KF, Fastenau JM, Mazonson PD, Falanga V. An economic assessment of Apligraf (Graftskin) for the treatment of hard-to-heal venous leg ulcers. *Wound repair and regeneration*, 2000; 8: 251-257.

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Sibbald RG, Torrance GW, Walker V, Attard C, MacNeil P. Cost- effectiveness of Apligraf in the treatment of venous leg ulcers. *Ostomy/wound management*, 2001; 47: 36-46.

Chang DW, Sanchez LA, Veith FJ, Wain RA, Okhi T, Suggs WD. Can a tissue-engineered skin graft improve healing of lower extremity foot wounds after revascularization? *Annals of Vascular Surgery*, 2000; 14: 44-49.

Citations About Promogran

Promogran matrix wound dressing is a primary dressing comprised of 55% collagen and 45% oxidized regenerated cellulose. It is produced by Johnson & Johnson Medical Limited (UK) and received FDA 510(k) premarket approval as substantially equivalent to Fibracol produced by the same company <http://www.fda.gov/cdrh/pdf/k014129.pdf> . Promogran is indicated for the management of exuding wounds including: diabetic ulcers, venous ulcers, ulcers caused by mixed vascular etiologies, full thickness and partial thickness wounds, donor sites and other bleeding surface wounds, abrasions, traumatic wounds healing by secondary intention, and dehisced surgical wounds

Veves A, Sheehan P, Pham Hau T. A randomized, controlled trial of Promogran (a collagen oxidized regenerated cellulose dressing) vs standard treatment in the management of diabetic foot ulcers. *Archives of Surgery*, 2002; 137: 822-827.

Ghatnekar O, Willis M, Persson U. Cost-effectiveness of treating deep diabetic foot ulcers with Promogran in four European countries. *Journal of wound care*, 2002; 11: 70-74.

Vin F, Teot L, Meaume S. The healing properties of Promogran in venous leg ulcers. *J Wound Care*, 2002; 11: 335-341.

Additional Information Relevant To VHA Patients

Reiber GE, Smith DG, Carter J, Fotieo G, Deery HG, 2nd, Sangeorzan JA, et al. A comparison of diabetic foot ulcer patients managed in VHA and non-VHA settings. *J Rehabil Res Dev*, 2001; 38: 309-317.

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